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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,845	02/09/2006	Rudolf-Giesbert Alken	82445	5014

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EXAMINER

VALENROD, YEVGENY

ART UNIT	PAPER NUMBER
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1621

MAIL DATE	DELIVERY MODE
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12/18/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,845

Applicant(s)

ALKEN, RUDOLF-GIESBERT

Examiner

YEVEGENY VALENROD

Art Unit

1621

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 34-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 34-55 is/are rejected.
- 7) ☒ Claim(s) 2-10 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The following is a final office action in application # 10/539,845.

Amendment to the claims filed 9/10/08 is acknowledged.

Remarks filed 9/10/08 have been fully considered by the examiner and are found insufficient to overcome the rejections of record. The text of the rejections from the previous office action is repeated below followed by Examiners reply to applicant's remarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

- (A) The breadth of the claims;
- (B) The nature of the invention;

(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant claims a method for the prophylaxis of psychoses using the compound of claim 1. The compound of claim 1 is a deuterated L-DOPA derivative. Dewar et al. (*Neuro-Psychopharmacology & Biological Psychiatry* **1985**, 9(5-6), 675-680) disclose a deuterated L-DOPA derivative D₃-DL-dopa, which is shown to work in a similar manner as L-DOPA. While L-DOPA is well known for its use in treatment of Parkinson disease and other diseases where it's necessary to increase the level of dopamine, use of L-DOPA for treatment of psychosis is not recognized in the art. In fact, the art teaches away from use of L-DOPA for treatment of psychosis. For example, Weiner et al. (*Neurology*, **2000**, 54(7), p1538) show that treatment of Parkinson's disease with L-DOPA induces Psychosis. There are no examples in the specification where applicant demonstrates treatment of psychoses using the compound of claim 1 or exemplifies involvement of compounds of claim 1 in a biological pathway which prior art has recognized as being involved with the onset of psychoses. Since Dewar et al have demonstrated that D₃-DL-dopa functions in a manner similar to L-DOPA, and D₃-DL-dopa is a compound of the instant invention, one

of ordinary skill would expect the deuterated derivatives of L-DOPA instantly claimed to aid in the onset of psychoses, and not have a therapeutic effect as is instantly claimed.

Reply to Applicant's Remarks concerning the rejection under 35 USC 112

Applicant has traversed the above rejection. The argument presented by the applicant can be summarized as:

1) The office has not met the burden of proof that the compounds of the instant invention are not effective in prophylaxis of psychoses (Remarks page 13 first paragraph)

2) Applicant has challenged the Weiner reference on: a) the compounds of Weiner are undeuterated L-DOPA used in treatment of Parkinsons where Psychosis is an adverse drug reaction. In contrast to applicant's deuterated derivatives, the compounds of the instant invention are only used for prophylaxis of schizophrenia (Remarks, paragraph 2, lines 3-6).

Examiner disagrees with the applicant.

1) Weiner reference was used to show that it is known in the art that L-DOPA causes onset of Psychosis. Although L-DOPA differs from the instant compounds in that it's not deuterated, Dewar reference was used to show that Deuterated L-DOPA functions in the same way as undeuterated. One skilled in the art would therefore draw a conclusion that deuterated L-DOPA derivatives would also cause onset of Psychosis. This is the evidence relied upon by the examiner to draw a conclusion of lack of enablement and it is believed to be sufficient to shift the burden of proof to the applicant.

2) Instant claims 49 – 55 are not limited to schizophrenia as applicant argues in the second paragraph on page 13 or the Remarks. The preamble to the claims states “A method for the prophylaxis of psychoses...”. Since L-DOPA has been shown by Weiner to result in onset of psychosis, and Dewar has indicated that the instantly claimed deuterated derivatives function in the same way as L-DOPA, it is reasonable to conclude that the instantly claimed compounds will result in onset of Psychosis when administered to a patient. Since Schizophrenia is a type of psychosis, it is a burden of the applicant to enable the use of the deuterated L-DOPA derivatives for prophylactic use in treatment of Schizophrenia.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 34-36 and 41 rejected under 35 U.S.C. 102(b) as being anticipated by Dewar et al. (*Neuro-Psychopharmacology & Biological Psychiatry* **1985**, 9(5-6), 675-680).

Dewar et al. disclose tri deuterated L-DOPA (D₃-DL-dopa), wherein the deuterium atoms are in α,α,β -positions of L-DOPA (page 675, lines 12-13 of the

Introduction). The disclosed compound meets the structural limitations of claims 1 and 11.

Dewar et al also disclose pharmaceutical compositions (page 676 Section titled "methods", paragraph 2). They disclose treating L-DOPA with HCl and NaOH which would invariably form salts with L-DOPA.

Dewar et al disclose administering D₃-DL-dopa to animals with pretreatment with decarboxylase inhibitor (Paragraph 3 of methods) and measuring dopamine concentrations (paragraph 4 of methods).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 34-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dewar et al. (*Neuro-Psychopharmacology & Biological Psychiatry* **1985**, 9(5-6), 675-680).

Scope of prior art

Dewar et al teach D₃-DL-dopa and its ability to replenish dopamine levels as is commonly practiced with L-DOPA (page 675, introduction, lines 1-2). Dewar et al also recognize the need to inhibit enzymes including decarboxylase (page 676, methods

paragraph 3), monoamine oxidase (page 677, discussion, paragraph 1) and β -hydroxylase (page 677, discussion paragraph 2). Dewar et al only utilize decarboxylase inhibitor in their experiments.

Ascertaining the difference between prior art and instant claims

Instant claims are directed to methods for treatment of dopamine deficiency disease. While Dewar et al demonstrate the ability of D₃-DL-dopa to increase levels of dopamine in rats (see page 677, figure 1), they do not disclose an actual method of treatment using D₃-DL-dopa.

Obviousness

One of ordinary skill in the art at the time the invention was made would have motivated by the disclosure of Dewar et al to utilize D₃-DL-dopa in treatment of dopamine deficiency diseases. Dewar et al. have demonstrated a faster rate of increase in dopamine concentration when compared to the L-DOPA (see figure 1). They have also recognized the need for enzyme inhibitors to inhibit the activity of β -hydroxylase, decarboxylase and monoamine oxidase. In order to avoid digestion of the D₃-DL-dopa by the enzymes one of ordinary skill would have been motivated to utilize inhibitors in treatment where D₃-DL-dopa is utilized and in pharmaceutical compositions comprising D₃-DL-dopa. Such inhibitors are known in the art (statement by the applicant in the specification, page 1 paragraph 3 through page 2 paragraph 2, is treated as admission of prior art). Combining D₃-DL-dopa with enzyme inhibitors to prepare pharmaceutical compositions and subsequent use of the said composition to treat dopamine deficiency diseases is therefore obvious.

***Reply to applicant's Remarks concerning the 102(b) and 103(a) rejections over
Dewar et al.***

Applicant has traversed the above art rejections. Applicant has argued that the amended claims are limited to "Substantially isolated Deuterated catecholamine derivative..." and that the Dewar reference fails to teach or suggest the compound of formula I, the L-enantiomer, in a substantially isolated state. The above argument is not found persuasive because the L-isomer is not a limitation of the instant claims. Applicant is arguing limitations not present in the claims. Applicant agrees that Dewar teaches D3-DL-dopa racemates. Since the claims are not directed to a single isolated isomer, Dewar meets the limitations of the instant claims as described in the rejection of record.

Claim objections

Claims 2-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Search of prior art has failed to uncover compound according to claims 2-10. Closest art is Dewar et al. (cited above), however Dewar et al. do not disclose compound where the phenyl ring is substituted with deuterium. Such a modification is not obvious.

Conclusion

Claims 1-11 and 34-55 are pending

Claims 1, 11 and 34-55 are rejected

Claims 2-10 are objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims

or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Y. Valenrod

/Paul A. Zucker/
Primary Examiner, Art Unit 1621